WHO guidelines on tuberculosis infection prevention and control

2019 update

THE END TB STRATEGY

World Health Organization

Summary of recommendations

Administrative controls

Recommendation 1: Triage of people with TB signs and symptoms, or with TB disease, is recommended to reduce *M. tuberculosis* transmission to health workers (including community health workers), persons attending health care facilities or other persons in settings with a high risk of transmission. *(Conditional recommendation based on very low certainty in the estimates of effects)*

Recommendation 2: Respiratory separation / isolation of people with presumed or demonstrated infectious TB is recommended to reduce *M. tuberculosis* transmission to health workers or other persons attending health care facilities. *(Conditional recommendation based on very low certainty in the estimates of effects)*

Recommendation 3: Prompt initiation of effective TB treatment of people with TB disease is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission. *(Strong recommendation based on very low certainty in the estimates of effects)*

Recommendation 4: Respiratory hygiene (including cough etiquette) in people with presumed or confirmed TB is recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission. *(Strong recommendation based on low certainty in the estimates of effects)*

Environmental controls

Recommendation 5: Upper-room germicidal ultraviolet (GUV) systems are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission. *(Conditional recommendation based on moderate certainty in the estimates of effects)*

Recommendation 6: Ventilation systems (including natural, mixed-mode, mechanical ventilation and recirculated air through high-efficiency particulate air [HEPA] filters) are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission. *(Conditional recommendation based on very low certainty in the estimates of effects)*

Respiratory protection

Recommendation 7: Particulate respirators, within the framework of a respiratory protection programme, are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission. *(Conditional recommendation based on very low certainty in the estimates of effects)*

Recommendation 5. Upper-room germicidal ultraviolet systems

Upper-room germicidal ultraviolet (GUV) systems are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Conditional recommendation based on moderate certainty in the estimates of effects)

The use of surgical masks may be poorly tolerated in severely ill patients. Therefore, health care authorities need to ensure the proper implementation of interventions within the hierarchy of controls for preventing *M. tuberculosis* transmission.

2.2. Environmental controls

To reduce the risk of transmission of *M. tuberculosis*, air can be made less infectious through the use of three principles: dilution, filtration and disinfection. Environmental controls are aimed at reducing the concentration of infectious droplet nuclei in the air. This is achieved by using special ventilation systems to maximize airflow rates or filtration, or by using germicidal ultraviolet (GUV) systems to disinfect the air. Ventilation systems can also be used to control the direction of airflow to reduce the spread of infection; for example, through the use of exhaust fans to generate negative pressure gradients. Environmental controls are used in combination with other IPC measures to help prevent the spread of *M. tuberculosis*.

Evidence and justification

A systematic review assessing the effectiveness of GUV systems yielded a total of five included studies, of which three evaluated IPC interventions involving health workers *(20, 24, 64)* (see Online annexes 4 and 5). Meta-analysis could not be performed, owing to differences in outcome measurement, and heterogeneity among the interventions.

One of the studies identified *(64)* suggested that the use of composite interventions, including placement of GUV light fixtures or luminaires in patient rooms and common areas, was associated with an 8.8% reduction in TST conversion among health workers. Another study evaluated whether use of GUV systems within TB laboratory units could substantially reduce the incidence of TB infection in health workers *(24)*. This study determined that the implementation of this intervention could contribute to an absolute risk reduction for LTBI of 14.8% among this population, and a reduction in the number of TB cases among health workers of 0.29 cases per 100 person-years. The third study was a retrospective cohort study that evaluated the effect of interventions to prevent *M. tuberculosis* transmission in health care facilities over a 10-year period *(20)*. The authors concluded that the use of mechanical ventilation, in combination with other environmental controls (including the use of GUV), was associated with a 4.1% reduction in TST conversion among health care staff.

The effectiveness of upper-room GUV systems in reducing LTBI and active TB disease in other persons attending health care settings or in settings with a high risk of *M. tuberculosis* transmission was also evaluated through the extrapolation of data from two studies in which infection was measured in animals, again using guinea-pigs as air samplers to measure the quantity of TB in the air *(65, 66)*. Both studies showed reduced rates of LTBI among guinea-pigs following GUV irradiation, compared with no irradiation of the air *(65, 66)*. The model evaluated in South Africa *(65)* demonstrated that 64.4% of the guinea-pigs in the control group compared with 17.7% of animals in the intervention group developed LTBI. The effect of the intervention in animals was extrapolated to a representative control population derived from nine studies where outcomes were measured in humans. Based on this calculation, the intervention would be expected to reduce the incidence of infection from 6.5% in the control group to 1.8% with the intervention – an expected absolute risk reduction of 4.7%. This represents a relative risk reduction of 72.4%. In the experimental model conducted in Peru *(66)*, 34.8% of animals in the control group developed

LTBI compared with 9.4% of animals in the intervention group breathing ward air when the UV lights were turned on in the ward. When extrapolated to the same control population, the intervention would be expected to reduce the incidence of infection from 6.5% to 1.8%, a relative risk reduction for TB infection of 72.9%.[1]

There is a growing body of evidence supporting the use of upper-room GUV systems as an effective intervention. The Guideline Development Group placed high value on the benefits presented in the included studies, and considered the evidence to be of moderate certainty for each of the comparisons. The group also acknowledged that – owing to the composite manner in which these IPC measures were implemented in the non-animal studies – it was difficult to discern the magnitude of effect associated with the use of upper-room GUV systems. Some members of the Guideline Development Group considered that the evidence warranted a strong recommendation; however, most of the group voted for the conditional recommendation (voting results: 5 for strong in favour, 11 for conditional in favour, 2 abstentions and 2 absentees). In making this recommendation, the panel emphasized that the effectiveness of such devices in destroying infectious agents would depend not only on the specifications of GUV fixtures themselves, but also on the appropriate selection of areas in which to install the devices, the quality of installation and maintenance, the duration of exposure to UV light (i.e. total exposure time) and the adequacy of air mixing.

Additionally, the panel recognized that the published observational studies in humans raised questions about the applicability of the intervention. For instance, GUV systems were implemented differently in different settings, with variation in unit types, in whether the system was used in conjunction with air-mixing devices and so on.

1 The methods used to infect guinea- pigs result in high levels of exposure, compared to with typical exposure in human populations. Consequently, the absolute proportion of animals with infection is expected to be higher in experimental animal studies than in human studies. In order to compare the findings in animals to with those in humans, the absolute risk difference in a human population was estimated by applying the relative risk in animals to a typical population (based upon the average infection incidence in nine studies). Therefore, both the expected absolute risk difference in humans and relative risk in guinea -pigs are presented for animal studies.

Implementation considerations

This recommendation is applicable for health care facilities as well as other congregate spaces with a high risk of *M. tuberculosis* transmission. In such settings, upper-room GUV systems should be implemented as part of a standard of care. The Guideline Development Group recognized that, because of cost considerations, the implementation of this intervention may not be feasible in all settings. Low- and middle-income countries that do not have the infrastructure or capacity to fully adopt this recommendation are advised to identify areas of higher risk of transmission, and prioritize the application of this intervention accordingly.

Success in the implementation of this intervention depends on appropriate installation, quality control and maintenance, to ensure that air disinfection occurs without adverse effects. Exceeding the threshold limit value[2] can lead to overexposure,[3] resulting in painful eye and skin irritation; hence, GUV systems must be monitored to ensure that optimal UV dose levels are achieved within a permissible limit of irradiance.

The IPC measures included in these guidelines should not be considered as individual interventions, but rather as a package. The Guideline Development Group recognized the role of upper-room GUV systems, but acknowledged that overreliance on these units as a single measure for IPC – especially without testing, maintenance and validation – may actually increase the risk of exposure to *M. tuberculosis*, defeating the purpose of such systems.

Upper-room GUV systems rely on air mixing between the upper and lower parts of a room. Thus, when implementing this intervention it

2 The American Conference of Governmental Industrial Hygienists (ACGIH) Committee on Physical Agents has established a threshold limit value for short-wavelength UV (UV-C) light exposure to avoid skin and eye injuries.

3 Air cleansing using GUV systems requires that persons in the treated space be shielded from excessive exposure to the UV radiation. To do so, the fixtures are shielded with louvres or bafflers in order to block radiation below the horizontal plane of the fixtures. Unshielded GUV lamps should be used only in areas that are not occupied, and safety features (e.g. switching device to deactivate the lamps in case the doors are opened) should be installed to ensure that overexposure to UVGI cannot occur.

is essential to consider factors that may affect the vertical air movement and transport of the infectious microorganisms to the upper portion of the room (e.g. use of simple fans to facilitate air movement in a room, temperature differential between the supply air and room air, mechanical ventilation rate and velocity of air out of ventilation diffusers).

Settings and target population

Upper-room GUV systems are suitable for all settings with a high risk of *M. tuberculosis* transmission, but particularly for those that have a significant burden of DR-TB.

In biological chamber studies, the effectiveness of upper-room GUV systems has been reported to decrease as humidity increases above 50–60% *(67)*. However, an evaluation of the efficacy of GUV for preventing transmission of *M. tuberculosis* using a guinea-pig air-sampling model demonstrated a protective effect in a setting where relative humidity was above 70% *(66)*. Additional considerations may be necessary in settings with high humidity (>70%), and the installation of systems with greater upper-room irradiance levels needs careful consideration.

Upper-room GUV systems are not feasible for use in household settings.

Resources

Although no cost or cost–effectiveness studies were analysed for this review, the Guideline Development Group recognized the variability in cost of upper-room GUV installations in different settings. The group emphasized that, in the long run, the cost of such systems may be justifiable, given the potential reduction in *M. tuberculosis* transmission (and the reduction in other airborne pathogens). However, the ability to justify this intervention will depend on the setting.

Because upper-room GUV systems rely on effective air mixing, it is necessary to ensure adequate air movement. Also, health care authorities must ensure proper allocation of resources for proper installation, running and maintenance and overall sustainability of this intervention.

Recommendation 6. Ventilation systems

Ventilation systems[a,b] (including natural, mixed-mode, mechanical ventilation, and recirculated air through high-efficiency particulate air [HEPA] filters) are recommended to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

(Conditional recommendation based on very low certainty in the estimates of effects)

Remarks

a The preference for specific ventilation systems is described under implementation considerations.

b The use of portable room-air cleaner appliances is not advised as a system to reduce *M. tuberculosis* transmission to health workers, persons attending health care facilities or other persons in settings with a high risk of transmission.

Evidence and justification

This systematic review sought to identify all relevant studies on five ventilation systems: natural ventilation, mechanical ventilation, mixed-mode ventilation, recirculated air filtration and room-air cleaner appliances. The systematic search yielded a total of only 10 observational studies, limited to the use of mechanical and mixed-mode ventilation. Eight of these studies evaluated the effect of using mechanical ventilation among health workers and others attending health care facilities or other settings with a high risk of *M. tuberculosis* transmission; six were before-and-after studies *(19–21, 42, 64, 68)*, one was a cohort study *(18)* and one was a case–control study *(69)* (see Online annexes 4 and 5). In addition, two studies – a prospective cohort study and a retrospective cohort study – evaluated the role of mixed-mode ventilation in protecting health workers *(24, 44)*.

Although the systematic search only identified applicable data on two ventilation systems (mechanical and mixed-mode ventilation), the Guideline Development Group decided to

extrapolate data to other ventilation systems and conduct a comparative analysis, based largely on data extrapolation and partially on expert opinion. The aim was to provide information on the use of technologies and systems that have been used in multiple settings for decades. This exercise allowed the Guideline Development Group to develop recommendations regarding the use of natural, mixed-mode, mechanical ventilation and recirculated air through HEPA filtration.

Given the absence of data on portable air cleaner appliances, the Guideline Development Group discussed the prospect of extrapolating available data to infer the potential effect of such devices on the incidence of LTBI and TB disease. However, given the suboptimal capacity[1] of most portable room-air cleaners, and consequently their limited capacity to provide the number of room-air exchanges required to decrease or eliminate the airborne infective agents, the panel decided not to extrapolate data from other ventilation systems to these portable devices.

In assessing available evidence, the Guideline Development Group acknowledged that meta-analyses could not be performed because of the heterogeneity between the included studies, and that results[2] of each study should be assessed individually. All but one of the studies *(18)* reported a reduction in incidence of LTBI, ranging from 2.9% to 11.5%. The longitudinal cohort study assessed the effect of negative pressure isolation rooms with HEPA filtration and 20 ACH in two tertiary care level hospitals in Brazil, comparing TST conversion rates among health workers with those in two other hospitals where environmental controls were not implemented in patient-care areas. The incidence of TST conversions was 7.4 per 1000 person-years and 8.1 per 1000 person-years in the two facilities where the measures were applied, compared with 12.2 per 1000 person-years and 19.8 per 1000 person-years in the two hospitals where the measures were not applied.

Studies reporting the use of mixed-mode ventilation showed reductions in the rate of LTBI among health workers when this intervention was implemented *(24, 44)*. However, the Guideline Development Group noted differences between the settings as well as the way in which interventions were implemented. The use of composite interventions, in addition to mechanical ventilation, in these studies can give rise to spurious associations. An association between the implementation of mechanical ventilation and an increase in TST conversions among other persons attending high -transmission risk settings was observed during an outbreak investigation at a university in Canada, suggesting that TB contacts attending class in mechanically ventilated rooms were more likely to be TST-positive than those in naturally ventilated rooms *(68)*. This effect could have been spuriously induced through residual confounding, or poor maintenance of mechanical ventilation systems leading to poorer overall ventilation. Also, naturally ventilated rooms may have had a higher ACH rate than rooms ventilated by mechanical systems.

The Guideline Development Group reviewed the evidence from the systematic reviews and discussed the limitations of included studies. Difficulties included dissecting the individual effect or impact of each intervention, and the lack of published studies regarding other forms of mechanical ventilation that have long been implemented in a variety of settings. Despite the lack of data, the panel was able to extrapolate from published studies to make decisions on specific interventions, such as natural and mixed-mode ventilation, and recirculated air filtration. Due to the limitations in the available evidence (discussed above), members of the Guideline Development Group decided that confidence in the evidence was to be rated "very low" because of concern about indirectness.

1 The use of portable air cleaners has been intended to be temporary in nature and not a substitute for any other ventilation system. Additionally, in settings where these devices may have been implemented, their use has been intended for small-sized rooms, because such devices do not have the airflow capacity to reach a minimum of 12 ACH. In the presence of more cost-effective alternatives for which there is long-term experience of use, and to avoid countries erroneously considering portable room-air cleaners as an equivalent ventilation system, the Guideline Development Group advised against the use of such devices unless further evidence on their impact becomes available.

2 The following results, as described here, represent the evaluation of mechanical ventilation systems; where results specific to mixed-mode ventilation are mentioned, this is made clear.

The Guideline Development Group further discussed and recognized the effectiveness of ventilation systems in providing sufficient dilution of particles in high-risk settings, and in effectively reducing the concentration of airborne *M. tuberculosis*. Although the panel agreed on the advantages that these systems confer – when properly installed according to room geometry, correctly monitored and properly maintained – there is a potential risk of paradoxically increasing the risk of transmission when systems are poorly implemented or poorly maintained. These factors led the group to emphasize the conditionality of this recommendation.

The results, once extrapolated, were used to compare and rank the various ventilation modes, bearing in mind the balance between desirable and undesirable effects, as well as other values and preferences. The Guideline Development Group considered that, in terms of function, natural, mixed-mode and mechanical ventilation systems can be equivalent, provided that they are properly designed, installed and maintained. The Guideline Development Group placed a high value on the overall benefit of natural ventilation, even though such ventilation depends on outdoor weather conditions and can have undesirable effects, such as variable direction and magnitude of airflow and the risk of contamination of adjacent rooms. The group ranked mechanically ventilated systems (mixed-mode) second in the comparative assessment, noting that such systems may inadvertently pose a greater hazard if they are poorly designed or not properly maintained. Although no cost–effectiveness studies evaluating mechanically ventilated and other environmental systems were available, the Guideline Development Group decided that mixed-mode ventilation systems were likely to be more affordable than fully mechanical modes or recirculated air filtration systems. The panel emphasized that while robust or highly specialized systems can reduce the concentration of infectious droplet nuclei in the air and thus prevent transmission, such systems may cause a false sense of reassurance, given the challenges in installation and maintenance, and the likelihood of human error in their implementation. In addition, the panel based their judgement on the assumption that, in resource-limited settings, highly specialized systems (e.g. mechanical ventilation systems and recirculated air through HEPA filters) would have a negative impact on equity and access, because they may not be adopted nationwide, being too expensive to install and maintain properly.

Overall, the preference for ventilation systems in resource-limited settings, based on available evidence of effectiveness and assumptions about financial constraints, was (in order of decreasing preference): (i) natural ventilation; (ii) mixed-mode ventilation; (iii) mechanical ventilation; and (iv) recirculated air with HEPA filtration (see Fig. 1). This order of preference may not be applicable in settings where resources are sufficient to procure and sustain more sophisticated systems, or where climatic conditions impede the use of natural or hybrid (mixed-mode) ventilation systems.

Lastly, given the variability of effectiveness in these systems, the Guideline Development Group continued to emphasize the complementarity of the three-level hierarchy of IPC, with a primary focus on administrative controls.

Fig. 1. Comparative assessment for the use of ventilation systems[a]

	Natural ventilation	Mixed-mode ventilation	Mixed-mode ventilation	Recirculated air with hepa filtration
Balance of effects	★★★★☆	★★★★☆	★★★★☆	★★★☆☆
Resources required	★★★★☆	★★★☆☆	★☆☆☆☆	★★☆☆☆
Cost effectiveness	★★★★★	☆☆☆☆☆	☆☆☆☆☆	☆☆☆☆☆
Equity	★★★★☆	★★★☆☆	★★☆☆☆	★★☆☆☆
Acceptability	★★★★★	★★★★☆	★★★★☆	★★★★☆
Feasibility	★★★★☆	★★★☆☆	★★☆☆☆	★☆☆☆☆

a Comparative assessment using a Likert-type model for comparison of interventions through the Grading of Recommendations Assessment, Development and Evaluation (GRADE) GRADEpro Guideline Development Tool (GDT) software. All the items in this scale use the five-point answer format, where the lower number of qualifiers (stars) indicates the least preferred system, based on data extrapolation and on individual judgements and perceptions of each member of the Guideline Development Group on feasibility, resources required and other criteria.

Implementation considerations

The decision on which system to use – natural ventilation, mixed-mode ventilation, mechanical ventilation or recirculated air with HEPA filtration – depends heavily on the needs of a particular setting, climate, cost–effectiveness assessment and sustainability of resources to ensure proper design and continued adoption of rigorous standards and maintenance.

The use of poorly designed or poorly maintained ventilation systems, leading to inadequate airflow, can result in health care-associated transmission of *M. tuberculosis*. Inadequate ventilation also increases the risk of transmission in other non-health care congregate settings such as correctional facilities, and refugee and asylum centres.

Programmes need to ensure the sustained use of ventilation systems that can provide sufficient dilution and removal of infectious particles. This can be achieved through proper commissioning of ventilation systems.

Settings and target population

Natural ventilation is the preferred ventilation system in resource-limited settings where there is high risk of *M. tuberculosis* transmission. However, the use of mixed-mode ventilation, mechanical ventilation or HEPA filters may be more appropriate in settings where natural ventilation is not suitable because of the climate (e.g. in cold climates) or other constraints. Natural ventilation is also the preferred system in settings with no constant electricity supply.

Resources

The effective implementation and functioning of ventilation systems requires allocation of sufficient resources to:

- conduct risk assessments to assess the direction of airflow or to relocate TB wards to the upper floors of buildings or downwind of non-TB wards; and
- install and maintain such systems in many health care and non-health care congregate settings.

The planning of and budgeting for ventilation systems also needs to consider the costs of regular assessment of ventilation performance